TISSUE REJUVENATION BY ILLUMINATING RADIATION

The present invention relates to tissue rejuvenation and in particular to tissue rejuvenation by means of selective production of collagen at a target site.

The human body has a variety of different types of collagen, which essentially constitute the extracellular matrix of the body. This matrix is the material that binds and supports cells and is essential for the survival of a multicellular organism. Collagens provide the tissue with tensile strength.

The various collagen containing structures in the body include bone, dentin, cartilage, uterus and the larger vessels in the circulatory system. As the body ages the rate of collagen naturally decreases leading to breakdown in tissue and organ structure and function. Other problems can also exacerbate or cause tissue or organ structure deterioration due to inhibition of collagen formation.

According to a first aspect, the invention comprises a technique for stimulating collagen containing structures, the technique comprising illuminating a target structure with illuminating radiation causing elevation of the temperature of a target structure, the radiation dosed to the target being controlled to induce a predetermined and precise inflammatory response in the target tissue.

The absorption of the radiation by the target structure at the predetermined low level controlled dose (resulting in the inflammatory response of the target structure tissue) stimulates collagen regrowth.

It is important that the radiation dose is controlled to ensure that overheating of the target tissue structure does not take place. Overdosing of energy (radiation) leads to thermal damage inhibiting the inflammatory phase resulting in less than optimum collagen formation. It is important therefore that the radiation energy dose delivered is of sufficiently low intensity and power to avoid tissue destruction. The radiation dose is therefore controlled dependent upon the body structure or tissue being illuminated but in all cases the intensity and duration of the illuminating radiation is relatively low level to prevent damage of the target structure or tissue.

The wavelength of the illuminating radiation is selected such that there is at least some absorption by the target structure or tissue.

In a preferred embodiment the radiation delivered is electromagnetic energy, preferably light, desirably substantially in the bandwidth 400-1500nm (more preferably substantially in the bandwidth 500-1000nm).

The illuminating radiation may be generated by laser, laser diode, light emitting diode, or a broad band white light source. The illuminating radiation is preferably of

a discrete wavelength or relatively narrow wavelength bandwidth. For a broad band white light source an appropriate filter is preferably provided.

Where the illuminating radiation is laser radiation, the laser may, for example comprises pulsed dye laser (585nm), an Argon Iron laser (514nm), Ti:Saphire laser (400nm-1100nm), Ruby laser(694nm), Nd:YAG laser (1064nm), or Frequency Doubled Nd:YAG laser (532nm).

a suitable laser diode would be a Gallium Arsenide laser diode at 630-690nm or 790-980nm.

LED's at wavelengths substantially in the range 550-1000nm would be suitable.

The technique can be used on a variety of body tissue structures either by means of direct external illumination of structures or by means of directing the illuminating radiation into the body (for example along a suitable waveguide) to be delivered to the site of the internal target structure.

According to a second aspect, there is provided apparatus for use in effecting refurbishment of tissue and/or tissue structures, which apparatus includes:

i) a source of illuminating radiation; and,

ii) means for directing the illuminating radiation

to a target site.

The means for directing the illuminating radiation to the target site preferably includes focussing means (for example optical focussing means). The means for directing the illuminating radiation to the target site preferably includes a flexible optical line including a distal portion through which the radiation is emitted in order to illuminate the target structure. The optical line may comprise an optical waveguide such as a length of fibreoptic.

The means for directing the illuminating radiation to the target site is preferably configured to permit manual manipulation enabling the zone of radiation impingement with the target site to be manually altered. Alternatively, the apparatus may be provided with an automated drive arrangement.

Desirably, the illuminating radiation is pulsed, preferably having a pulse duration substantially in the range 1 microsecond-100ms. Alternatively, scanning of illuminating radiation can produce a similar effect, in that localised tissue is irradiated only for the required short time period to deliver the appropriate energy dose.

The invention will now be further described in specific embodiments by way of example only, and with reference to the accompanying drawings, in which:

Figure 1 is a schematic representation of a first embodiment of a technique according to the invention,

Figure 2 is a schematic representation of a second embodiment of a technique according to the invention;

Figure 3 is a schematic representation of a further embodiment of a technique according to the invention;

Figure 4 is a schematic representation of a further embodiment of a technique according to the invention;

Figure 5 is a schematic representation of a further embodiment of a technique according to the invention; and,

Figure 6 is a schematic representation of a further embodiment of a technique according to the invention.

Referring to the drawings, and initially to Figure 1, there is shown a tissue rejuvenation technique in which an arrangement 1 includes a light source 2, such as an LED, laser diode or other laser or a white light source (provided with an appropriate filter), having a wavelength in a narrow bandwidth in the range 550-1000nm, directs a beam 3 via focussing optics 4 into a fibreoptic waveguide 5. Light emitted from the distal end of fibreoptic waveguide 5 passes through a collimating lens 6 where it is directed to illuminate the surface of a tissue structure 7.

In the embodiment shown in Figure 2, the beam 3 emitted from light source 2 passes directly through a focussing lens 16 which focusses the beam onto the tissue structure 7.

In the embodiment shown in Figure 3, the beam 3 from the light source 2 is directed to a scanning optical arrangement comprising rotating scanning mirrors 9, 10 arranged to scan the beam in orthogonal X-Y directions onto the tissue 7.

In each of the embodiments shown in Figures 1 to 3, the relevant tissue structure 7 is directly illuminated from externally of the body (extra-corporeal illumination).

The intensity and duration of the light beam illuminating the tissue 7 is controlled such that the energy dosed to the tissue is at a level where collagen formation is promoted, without the tissue being "injured" to a degree at which structural integrity of the tissue deteriorates. Illumination promoting collagen production mirroring wound healing in the inflammatory, proliferate and remodelling phases results in collagen production and enhancement of the structural integrity of the tissue.

It is important that the wavelength of the light illuminating the tissue is selected to have at least a component which is selectively absorbed to the required degree by the tissue in question. Appropriate selection of the wavelength to be absorbed by the tissue, or a

chromophore at or below the tissue surface, can enable discrete target sites at or below the tissue surface to be targeted.

The arrangements shown in Figure 4 to 6 relate to interstitial rejuvenation techniques where an extra corporeal light source 2 produces a beam 3 which can be directed through the body surface interface to target an internal cell structure 11, 12.

In the embodiment shown in Figure 4, the light beam 3 is focussed into a fibreoptic waveguide 5 which extends through a sheathing catheter 13. Light emanating from the end of fibreoptic waveguide 5 illuminates the target structure 11 below the body surface 14.

In the embodiments shown in Figures 5 and 6, the fibreoptic waveguide 5 extends into and along a target vessel 12 which comprises the circulatory system of the body (such as for example an artery).

In the embodiment of Figure 5, light is reflected from a mirror end 15 to illuminate the desired "target" portion of the internal vessel wall 12.

In the embodiment shown in Figure 6, the fibreoptic waveguide 5 is provided with a diffusing end 16 arranged to diffuse the light to illuminate radially the entire "target" portion of the vessel wall 12.

Illumination of the relevant tissue target structure with illuminating radiation of the required wavelength and dosage produces the inflammatory/wound healing response promoting the maximum degree of collagen formation. Promotion of collagen at the target site effectively rejuvenates the target tissue/structure.

To test the efficacy of the invention, examples have been performed using laser radiation and measuring terminals of Type III collagen produced.

When Type III collagen is formed, the molecule is in the form of a long chain with two terminals on either end. When three collagen molecules have been produced, the molecules bond together and the terminals on either end of the chain separate and are released into the dermal interstitial fluid. By measuring the quantity of the terminals in the fluid, the rate of collagen production can be measured.

As an example of the technique, biochemical investigations have shown that the production rate of Type III collagen in the dermal region of the skin can be increased by the application of the following laser parameters:

Wavelength:	585nm
Pulse Duration:	350μsec
Energy Density:	2.4J/cm^2
Spot Size:	5mm Diameter

delivered to the surface of the skin via a flexible fibre optic.

When the skin was irradiated with these parameters, the production rate of Type III collagen in the skin increased by 84%.

Similar tests performed with a Frequency Doubled Nd:YAG laser operating at the following parameters:

Wavelength:	532nm
Pulse Duration:	2msec to 20msec
Energy Density:	2-20J/cm^2
Spot Size:	3mm (dia)

showed an increase of between 22% and 44% in the Type III Collagen production rate.

Both tests were performed by treating a selected area of skin with the prescribed laser parameters and waiting 72 hours before raising suction blisters on the treated and untreated control areas. The interstitial fluid collected from the suction blisters was analysed using an immunoflourescent technique to measure the quantity of the amino-propeptide terminal of the Type III collagen molecule (PIIINP).

The quantity of PIIINP found in the blister fluid is related to the amount of Type III collagen being produced at the investigation site. The percentage increase

figures quoted are relative to adjacent control sites.